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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/472,558	12/27/1999	MOHAMMAD B. BAHRAMIAN	2281/102	8925

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EXAMINER
PARAS JR, PETER

ART UNIT	PAPER NUMBER
2632	28

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/472,558	Applicant(s) BAHRAMIAN ET AL
	Examiner Peter Paras	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2002 and 02 March 1996* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,13-18,26-49,51 and 53-67* is/are pending in the application.

4a) Of the above claim(s) *28-49,51 and 53-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,13-18,22-25 and 57-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice To Comply* .

Applicant's amendment received on 5/30/02 has been entered. Claims 11, 14, 17, and 23 have been amended. New claims 57-65 have been added.

Applicant's supplemental amendment received on 6/3/02 has been entered. New claims 66-67 have been added.

Claims 11, 13-18, 22-25, 28-49, 51, and 53-67 are pending. Claims 11, 13-18, 22-25 and 57-67 are under current examination.

Election/Restrictions

Claims 28-49, 51, and 53-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 5.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached **N**otice To Comply With Requirements For Patent Applications Containing **N**ucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. *Any* response to this Office Action, which fails to meet all of these requirements, will be considered non-responsive. The nature of the noncompliance with

the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Applicant is requested to return a copy of the attached **N**otice to Comply with the response.

To avoid damage to a CRF by irradiation, a reply to a notice to comply with the sequence rules should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>**, EFS Submission User Manual - ePAVE)
2. Mailed to: **U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202**
3. Mailed by Federal Express, United Parcel Service or other delivery service to: **U. S. Patent and Trademark Office, 2011 South Clark Place, Customer Window, Box Sequence, Crystal Plaza Two, Lobby, Room 1B03, Arlington, Virginia 22202**
4. Hand Carried directly to the Customer Window at: **2011 South Clark Place, Crystal Plaza Two, Lobby, Room 1B03, Box Sequence, Arlington, Virginia 22202**

Drawings

New corrected drawings are required in this application because the drawings as filed are objected to the by the draftsman as set forth in the PTO 948 mailed on 7/18/00. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

The previous objection to claim 17 has been withdrawn in view of Applicant's claim amendments.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 13-18, 22-25, and 57-67 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of muting expression of a α1(I) procollagen in cultured rodent fibroblasts, comprising introducing a plasmid containing a portion of the α1(I) procollagen nucleotide sequence identified as a muting nucleotide sequence, wherein the plasmid is transiently transfected into the rodent fibroblasts and the nucleotide sequence of endogenous α1(I) procollagen is not disrupted, wherein the α1(I) procollagen sequence is identified by screening nucleotide fragments of the endogenous gene to identify muting sequences, does not reasonably provide enablement for the claimed method comprising other embodiments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record advanced on pages 2-11 of the Office action mailed on 1/30/02.

Applicant's arguments filed 5/30/02 have been fully considered but they are not persuasive. Applicants disagree with the Examiner's position that "In the absence of any relevant teachings with respect to the mechanism of muting the skilled artisan cannot predict how to achieve muting of other genes. As such guidance is lacking in the instant specification that teaches the skilled artisan how to construct and use other muting nucleic acid sequences." Applicants assert that the instant specification has taught that identification of muting nucleic acid compositions requires screening different fragments of DNA from the targeted gene. Applicants have pointed to the specification on pages 4, 5-7, and 31-33 for support of identification of muting nucleic acid sequences. See the amendment on pages 5-6.

In response, the Examiner acknowledges that the specification contemplates screening of random DNA fragments as a means of identifying muting sequences. First, the steps for identifying muting sequences (for example, screening fragments) are not recited by the instant claims. However, the specification has not provided any working examples that demonstrate muting of any nucleic acid sequences other than the α1(I) procollagen gene. Further, there is no teaching provided by the evidence of record that would suggest whether the muting effect is general, so that it could be applicable to any other gene, or whether the muting effect is only specific to α1(I) procollagen as the mechanism for the muting effect has not been disclosed. The fact that the specification has provided a prophetic example of how the tat gene or an immunoglobulin gene may be muted does not in any way enable the breadth of the claims; there is no evidence of record that demonstrates muting of those genes when

practicing the method as claimed. In fact, a single working example directed to muting of a single gene, α1(I) procollagen gene, cannot be extrapolated to embrace muting of all genes as claimed. See page 5-6 of the Office action mailed on 1/30/02.

Applicants also assert that the Examiner has wrongly assumed that if the muting nucleic acid is RNA or a nucleic acid analog is selected or screened. Applicants further assert that the selecting of muting nucleic acid sequences is done at the DNA level but that only a sequence analogous to the selected sequence is introduced into the cultured cells. It would appear that Applicants are suggesting that once a DNA sequence has been selected that it can be transcribed into RNA or converted into a DNA analog and then transfected. See pages 6-7 of the amendment.

In response, the Examiner asserts that the evidence of record has only provided a single working example, where DNA sequences were used as muting sequences. The are no teachings, guidance, or working examples provided by the evidence of record that suggest muting is achieved with RNA or DNA analogs to support the breadth of the claims to that end. In fact the nature of the invention is unknown or otherwise undeveloped as no explanation of the mechanism of muting can be provided. There is no support provided by the evidence of record that teaches that RNA or a DNA analog can achieve muting of a target gene. Moreover, the specification does not contemplate converting a selected DNA sequence into RNA or a DNA analog prior to introducing such into a cultured cell to achieve muting.

Applicants assert that the exogenous collagen sequences are neither transcribed nor expressed as a protein. See the amendment on page 7.

In response, the Examiner acknowledges Applicants explanation.

Applicants submit that claim 23 as amended is directed to a 3' portion of the endogenous gene. Applicants go on to argue that there is no requirement that the exogenous gene be transcribed to see muting. Applicants further argue that double-stranded RNA can be produced *in vitro* and that any synthesized RNA molecule can comprise a 3' coding portion of the endogenous gene. Finally, Applicants argue that muting ds RNA can arise from within the cell itself, but not from transcription of the exogenous gene, the production of which is triggered by delivery of the exogenous muting DNA sequence. See the amendment on pages 7-8.

In response, the Examiner acknowledges that claim 23 has been amended. But the claim as written does not encompass synthesizing RNA *in vitro* and then delivering it. The claim as written encompasses regions of the endogenous gene but requires that the muting nucleic acid is homologous to the regions of the endogenous gene. Reading the claim as written suggests that the nucleic acid molecule, RNA included, comprises 3' untranscribed regions. There is no indication that if the RNA molecule is the muting nucleic acid, then it is synthesized *in vitro* prior to transfection. See page 8 of the Office action mailed on 1/30/02.

Applicants assert that the instant specification has provided more than enough guidance for identifying muting sequences. Applicants argue that the muting effect is gene specific and that the muting nucleic acid sequence can be identified by screening of random fragments of the target gene. Applicants emphasize that screening for

muting sequences is a required element of the claimed invention. See the amendment on page 9.

In response, the Examiner asserts that the process of identifying muting nucleic acid sequences (i.e. screening) is not required by the claim although Applicants continue to assert its importance. The Examiner suggests amending the claims to include identification of muting nucleic acid sequences by screening (in appropriate claim language). Inclusion of the screening process in the claims may be sufficient to overcome the aspect of identification of muting sequences in the instant enablement rejection. Failure to include the screening process in the claims results in speculation of how to identify the muting sequences.

Applicants argue that use of attenuated bacteria as a vehicle for to deliver muting nucleic acid sequences to a population of cultured cells is efficient and enabled. Applicants also assert that the Examiner's reasoning regarding attenuated bacteria is in error. See the amendment on pages 10-11.

In response, the Examiner maintains that the use of attenuated bacteria as a vehicle for delivering muting nucleic acid sequences to a population of cultured cells to achieve muting of a target gene in the population as a whole is not supported by the evidence of record. See the Office action of 1/30/02 on page 11 at the top. There are no working examples provided by the instant specification that demonstrate muting of a target gene in a whole population of cultured cells, as required by the claims, when attenuated bacteria are used to deliver muting nucleic acid sequences. The facts regarding DNA delivery by attenuated bacteria have been clearly presented on pages 9-

10 of the Office action of 1/30/02. See Grillot-Courvalin and Dietrich. Applicants appear to be relying on a statement made by Grillot-Courvalin that suggests efficient delivery of nucleic acid sequences to mammalian cells in support of their arguments. Grillot-Courvalin presents data that suggests that small percentages of mammalian cells are transfected by attenuated bacteria, wherein the percentage of transfected cells ranges from 0.3 to 20%. See pages 862, page 863 (Table 1), page 864 (Table 3) and page 865 at the top. Dietrich corroborates the data of Grillot-Courvalin by reporting a transfection efficiency of 0.3% in macrophages. See page 10 of the Office action mailed on 1/30/02. It should be made of record that Applicants claims are directed to muting expression of a target gene in a population of cultured cells as a whole however the evidence made of record by the Examiner as discussed above clearly suggests that a low percentage (as low as 0.3%, for example) of mammalian cells are actually transfected with attenuated bacteria. In light of such a low percentage of transfected cells it would be unpredictable to achieve muting over the population of cells as a whole when practicing the claimed invention with attenuated bacteria. Further, the instant specification has not provided any working examples that would provide any evidence to the contrary; not a single working example directed to attenuated bacteria has been provided by the instant specification. Attenuated bacteria were only mentioned in passing by the instant specification, and no guidance for carrying out such an embodiment was provided in the specification.

Accordingly, the previous rejection is maintained for the reasons of record and as discussed in the preceding paragraph.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejections of claims 17-18 and 22-23 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11, 13-18, 22, 24, and 66 as amended, originally filed, or newly added are rejected under 35 U.S.C. 102(b) as being anticipated by Guimaraes. The previous rejection is maintained for the reasons of record advanced on pages 13-15 of the Office action mailed on 1/30/02.

Applicant's arguments filed 5/30/02 have been fully considered but they are not persuasive. Applicants are of the opinion that the rejection with the Guimaraes reference is improper for the following reasons: 1) Guimaraes does not teach that Sps2 is endogenous to monkey cells; 2) the claim requires identifying a muting nucleic acid composition; and 3) Guimaraes teaches expression of the exogenous DNA

introduced into the COS-7 cells while the instant claims do not require expression of the exogenous muting nucleic acid sequences. See pages 14-18 of the amendment.

In response, the Examiner maintains that Guimaraes anticipates the invention as claimed. First, Guimaraes has taught that Sps2 has been isolated from mice and humans. This leads one to believe that Sps2 at a minimum is a mammalian gene unless evidence to the contrary is provided. As such one ordinary skill would expect that Sps2 would be found in monkey cells. Next the claim requires identification of a muting nucleic acid composition. The term muting is not considered to be relevant for the purposes of this rejection as it merely is an intended use limitation. The claim has been interpreted to require only identification of a nucleic acid composition that is homologous to an endogenous sequence. Guimaraes clearly identified the DNA sequence to be transfected and as argued above there is no credible reason to believe that Sps2 is not endogenous to monkey cells. Finally, in light of the above reasoning the argument can be made that because a homologous sequence has been identified and introduced into a cultured population of animal cells that muting of the endogenous Sps2 gene must have been achieved, if, as Applicant contends, muting is a general phenomenon. There is no reason to believe that muting could be achieved by the presence alone of the exogenous Sps2 gene and that this effect is independent of expression of the exogenous Sps2 gene in the absence of evidence to the contrary. The events of muting of the endogenous Sps2 gene and expression of the exogenous Sps2 gene are independent and separate. The presence alone of exogenous Sps2 sequences is sufficient to mute expression of endogenous Sps2. As argued by

Applicants, it appears that the identification process is important to the invention. The Examiner understands this point and recommends that identification steps be included in the claims. Amending the claims to that end may be sufficient to overcome this rejection.

Accordingly, the rejection is maintained for the reasons of record and as discussed above.

Claims 11, 13-18, 24-25, 57-62, 65-67 as amended, originally filed, or newly added are rejected under 35 U.S.C. 102(b) as being anticipated by Chan et al. The previous rejection is maintained for the reasons of record advanced on pages 20-21.

Applicant's arguments filed 5/30/02 have been fully considered but they are not persuasive. Applicants argue that the Chan reference is not relevant to the claimed invention for the following reasons: 1) Chan does not teach identification of a muting nucleic acid sequence; and 2) Chan teaches expression of exogenous nucleic acid sequences. See page 18 of the amendment.

In response, the Examiner maintains that Chan anticipates the invention as claimed. The claim requires identification of a muting nucleic acid composition. The term muting is not considered to be relevant for the purposes of this rejection as it merely is an intended use limitation. The claim has been interpreted to require only identification of a nucleic acid composition that is homologous to an endogenous sequence. Chan has identified the sequences to be transfected. In light of the above reasoning the argument can be made that because a homologous sequence has been

identified and introduced into a cultured population of animal cells that muting of the endogenous collagen gene must have been achieved, if, as Applicant contends, muting is a general phenomenon. There is no reason to believe that muting could be achieved by the presence alone of the exogenous collagen gene sequences and that this effect is independent of expression of the exogenous collagen gene sequences in the absence of evidence to the contrary. The events of muting of the endogenous collagen gene and expression of the exogenous collagen gene are independent and separate. The presence alone of exogenous collagen sequences is sufficient to mute expression of endogenous collagen. As argued by Applicants, it appears that the identification process is important to the invention. The Examiner understands this point and recommends that identification steps be included in the claims. Amending the claims to that end may be sufficient to overcome this rejection.

Accordingly, the rejection is maintained for the reasons of record and as discussed above.

Claims 11, 13-18, 22, 24, 57-62, 65-67 rejected under 35 U.S.C. 102(b) as being anticipated by Rippe. The previous rejection is maintained for the reasons of record advanced on pages16-18.

Applicant's arguments filed 5/30/02 have been fully considered but they are not persuasive. Applicants have argued that Rippe has not identified a muting nucleic acid sequence. See page 18 of the amendment.

In response, the Examiner maintains that Rippe anticipates the invention as claimed. The claim requires identification of a muting nucleic acid composition. The term muting is not considered to be relevant for the purposes of this rejection as it merely is an intended use limitation. The claim has been interpreted to require only identification of a nucleic acid composition that is homologous to an endogenous sequence. Rippe has identified the sequences to be transfected. In light of the above reasoning the argument can be made that because a homologous sequence has been identified and introduced into a cultured population of animal cells that muting of the endogenous collagen gene must have been achieved, if, as Applicant contends, muting is a general phenomenon. There is no reason to believe that muting could be achieved by the presence alone of the exogenous collagen gene sequences and that this effect is independent of expression of the exogenous collagen gene sequences in the absence of evidence to the contrary. The events of muting of the endogenous collagen gene and expression of the exogenous collagen gene are independent and separate. The presence alone of exogenous collagen sequences is sufficient to mute expression of endogenous collagen. As argued by Applicants, it appears that the identification process is important to the invention. The Examiner understands this point and recommends that identification steps be included in the claims. Amending the claims to that end may be sufficient to overcome this rejection.

Accordingly, the rejection is maintained for the reasons of record and as discussed above.

Claims 11, 13-17, 22-23, 57-61, 63-65, and 66-67 as originally filed, amended, or newly added are rejected under 35 U.S.C. 102(b) as being anticipated by Slack. The previous rejection is maintained for the reasons of record advanced on pages 18-19 of the Office action mailed on 1/30/02.

Applicant's arguments filed 5/30/02 have been fully considered but they are not persuasive. Applicants have argued that Slack has not identified a muting nucleic acid sequence and teaches expression of an exogenous gene. See page 19 of the amendment.

In response, the Examiner maintains that Slack anticipates the invention as claimed. The claim requires identification of a muting nucleic acid composition. The term muting is not considered to be relevant for the purposes of this rejection as it merely is an intended use limitation. The claim has been interpreted to require only identification of a nucleic acid composition that is homologous to an endogenous sequence. Slack has identified the sequences to be transfected. In light of the above reasoning the argument can be made that because a homologous sequence has been identified and introduced into a cultured population of animal cells that muting of the endogenous collagen gene must have been achieved, if, as Applicant contends, muting is a general phenomenon. There is no reason to believe that muting could be achieved by the presence alone of the exogenous collagen gene sequences and that this effect is independent of expression of the exogenous collagen gene sequences in the absence of evidence to the contrary. The events of muting of the endogenous collagen gene and

expression of the exogenous collagen gene are independent and separate. The presence alone of exogenous collagen sequences is sufficient to mute expression of endogenous collagen. As argued by Applicants, it appears that the identification process is important to the invention. The Examiner understands this point and recommends that identification steps be included in the claims. Amending the claims to that end may be sufficient to overcome this rejection.

Accordingly, the rejection is maintained for the reasons of record and as discussed above.

Claims 11, 13-18, 22, 24, and 66 as amended, originally filed, or newly added are rejected under 35 U.S.C. 102(b) as being anticipated by Gamborotta et al. The previous rejection is maintained for the reasons of record advanced on pages 15-16 of the Office action mailed on 1/30/02.

Applicant's arguments filed 5/30/02 have been fully considered but they are not persuasive. Applicants have argued that the method of Gamborotta does not teach muting of endogenous gene expression at the transcriptional and post-transcriptional levels. See the amendment on pages 20-23.

In response, the Examiner maintains that Gamborotta anticipates the invention as claimed. It appears that Applicants have included the limitations of transcription and post-transcription in an attempt to overcome the instant rejection. It appears that the muting phenomenon occurs at the level of transcription. Clearly, the method of

Gamborotta affects gene expression at the level of transcription. Next, when gene expression at the level of transcription is affected, then gene expression at the post-transcriptional level must also be affected in the absence of evidence to the contrary. This analysis is applicable as the mechanism by which muting occurs has not been disclosed by the evidence of record. In this case there does not appear to be any convincing reason that events at the levels of transcription and post-transcription should be separated.

Accordingly, the rejection is maintained for the reasons of record and as discussed in the preceding paragraph.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Patsy Zimmerman whose telephone number is (703) 308-0009.

Peter Paras, Jr.

Art Unit 1632

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Application No.:09472,558

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

[X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

[X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

[X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

[ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

[ ] 7. Other: _____

Applicant Must Provide:

[X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

[X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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